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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,569	11/29/2005	Michael Betz	BPG-32574A/BCK	5279

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EXAMINER	
SCHLIENTZ, NATHAN W	
ART UNIT	PAPER NUMBER
1616	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,569	BETZ ET AL.	
	Examiner	Art Unit	
	Nathan W. Schlientz	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,7-9,11,12,14,15,22,23,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,7-9,11,12,14,15,22,23 and 25* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/25/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2, 18-20 and 24 have been cancelled and claim 26 has been newly added by Applicant in an amendment filed 09 November 2007. As a result, claims 1, 3, 5, 7-9, 11, 12, 14, 15, 22, 23, 25 and 26 are examined herein on the merits for patentability. No claim is allowed at this time.

Claim Objections

Claim 26 is objected to as being dependent upon a cancelled base claim. Claim 26 is currently dependent upon claim 2, which was cancelled in the aforementioned amendment.

Withdrawn Rejections

The rejection of claim 1, 2 and 24 under 35 U.S.C. 103(a) as being unpatentable over 5,763,394 (O'Connor et al.) is hereby withdrawn by the examiner in view of the aforementioned cancellation of claims 2 and 24.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 3, 5, 7-9, 11, 12, 14, 15, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,763,394 (hereinafter O'Connor et al.).

The instant claims are drawn to a multi-dosage liquid pharmaceutical formulation of human growth hormone (hGH) consisting essentially of:

a) about 6 mg/ml to about 14 mg/ml hGH,
b) about 2 mg/ml to about 5 mg/ml phenol,
c) about 10 mM aqueous buffer, and
d) about 0.05 to about 4 mg/ml non-ionic surfactant, and

wherein the formulation has a tonicity of from about 100 mOsm/kg to about 500 mOsm/kg, pH of from about 6.1 to about 6.3, and is substantially free of an amino acid excipient. Preferably, the aqueous buffer is a phosphate, citrate, acetate, or formate buffer and the non-ionic surfactant is poloxamer 188 or a polysorbate. Most preferably, the aqueous buffer is a phosphate buffer and the non-ionic surfactant is poloxamer 188.

O'Connor et al. disclose a stable, pharmaceutically acceptable, aqueous formulation of human growth hormone comprising hGH, a buffer, a non-ionic surfactant, and *optionally* a neutral salt, mannitol and a preservative (Abstract; col. 2, ll. 28-32; and col. 3, ll. 62-63).

O'Connor et al. disclose a human growth hormone formulation consisting essentially of (claim 9):

a) 1mg/ml to 20 mg/ml hGH,
b) a preservative,
c) a buffer system to provide a pH of 5.5 to 7,
d) 0.1% w/v to 1% w/v non-ionic surfactant, and
e) 50 mM to 200 mM neutral salt.

O'Connor et al. further disclose the buffer is selected from the group consisting of citrate, phosphate and acetate buffers (claim 16), and is most advantageously in the range of about 2 mM to about 50 mM (col. 3, ll. 46-48). O'Connor et al. further disclose the non-ionic surfactant is poloxamer 188, poloxamer 184, or polysorbate (claims 11

and 12). O'Connor et al. further disclose that the preferred preservatives include 0.2-0.4%% w/v phenol (col. 3, ll. 54 and 55; and claim 17).

O'Connor et al. further disclose a directly injectable hGH formulation consisting essentially of:

a) 5mg/ml hGH,
b) 0.5 mg/ml phenol,
c) 2.5 mg/ml sodium citrate (aqueous buffer),
d) 2.0 mg/ml polysorbate 20 (non-ionic surfactant), and
e) 8.8 mg/ml sodium chloride (neutral salt/tonicity agent),

wherein the hGH formulation is at a pH of 6 (claim 18).

O'Connor et al. further disclose an hGH formulation containing:

a) 5mg/ml hGH,
b) 0.25% w/v phenol,
c) 10 mM sodium citrate (aqueous buffer),
d) 0.1% w/v poloxamer 188 (non-ionic surfactant), and
e) 50 mM mannitol (tonicity adjusting agent).

wherein the hGH formulation is at pH 6.0 (col. 7, ll. 58-67; and Table 3, Formulation 52).

O'Connor et al. further disclose that the neutral salts concentration is adjusted to near isotonicity, depending on the other ingredients present in the formulation (col. 4, ll. 1-5).

Therefore, for the aforementioned reasons, O'Connor et al. fully anticipate all the limitations of the instant claims.

Response to Arguments

Applicant's Remarks filed 09 November 2007 have been fully considered but they are not persuasive. Applicants argue on page 5 that by using the narrowing language "consisting essentially of", the present claims preclude the presence of additional

excipients such as neutral salt and/or mannitol, which Applicants argue are necessary components of the O'Connor et al. formulations. Applicants argue that there is no basis for concluding either that the inclusion of the non-ionic surfactant is alone sufficient, or that the inclusion of either mannitol or a neutral salt is not required to achieve the beneficial results of the invention, as disclosed by O'Connor et al.

However, the examiner respectfully disagrees. As mentioned by Applicants, O'Connor et al. clearly disclose that the neutral salt, mannitol and preservative are optional ingredients, and thus are not required (Abstract; col. 2, ll. 28-32; and col. 3, ll. 62-63). The examiner respectfully directs attention to MPEP 2123(I) and (II):

> "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)).
>
> A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including non-preferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005); *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed.").
>
> Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments. *In re Susi,* 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Furthermore, "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Therefore, O'Connor et al. disclose a stable, pharmaceutically acceptable, aqueous formulation of human growth hormone comprising hGH, a buffer and a non-ionic surfactant, wherein a neutral salt, mannitol, or a preservative may or may not be added.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over O'Connor et al.

Applicant claims:

The Applicant claims a kit comprising an injection device and a separate container containing a multi-dosage liquid formulation of hGH according to claim 1.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The teachings of O'Connor et al. are described above. Essentially, O'Connor et al. teaches hGH formulations consisting of from about 1 mg/ml to about 20 mg/ml hGH, phenol, aqueous buffer, and non-ionic surfactant at a pH of from about 5.5 to about 7.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

O'Connor et al. do not explicitly teach a kit comprising the hGH formulation and an injection device. However, O'Connor et al. do teach a method for using their hGH formulation comprising formulating their composition in a pharmaceutically acceptable, injectable sterile aqueous vehicle, storing said formulation, and directly injecting the stored formulation into a patient (claims 20-23). O'Connor et al. also teach that the preservative is included in the formulation to retard microbial growth and thereby allowing "multiple use" packaging of the hGH (col. 2, ll. 24-25; col. 3, ll. 50-52; and claim 19).

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to prepare a "multiple use" package, or kit, comprising the hGH formulation taught by O'Connor et al., wherein the kit comprises an injectable device and a container with a multi-dosage liquid formulation of hGH because O'Connor et al. teach storing their hGH formulation in a "multiple use" package followed by injecting the formulation into a patient.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's Remarks filed 09 November 2007 have been fully considered but they are not persuasive. Applicants argue on pages 7-8 that to the extent that the method taught in O'Connor et al. could be considered to require the use of an injectable device and a container to store the hGH formulation, there is nothing to suggest that these are present as a kit as instantly claimed.

However, O'Connor et al. teach that the preservative is included in order to allow "multiple use" packaging of the hGH formulations (col. 2, ll. 24-25; col. 3, ll. 50-52; and claim 19). O'Connor et al. also clearly teach a method for using their hGH formulation

comprising formulating their composition in a pharmaceutically acceptable, injectable sterile aqueous vehicle (i.e. "multiple use" packaging), storing said formulation, and directly injecting the stored formulation into a patient (claims 20-23). Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to include an injection device with the "multiple use" packaging of hGH because O'Connor et al. teaches that the formulation are injected into the patient. Thus, the instantly claimed kit is not a patentably distinct invention to distinguish it from O'Connor et al.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is 571-272-9924. The examiner can normally be reached on 8:30 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NWS

/Mina Haghighatian/
Primary Examiner
Art Unit 1616